Causation

WSA Consensus Overview
October 2000

PM3006848066

Source: https://www.industrydocuments.ucsf.edu/docs/ytlx0001

Cigarette Smoking and Disease in Smokers: We agree with the overwhelming medical and scientific consensus that cigarette smoking causes lung cancer, heart disease, emphysema and other serious diseases in smokers. Smokers are far more likely to develop serious diseases, like lung cancer, than non-smokers. There is no "safe" cigarette. These are and have been the messages of public health authorities worldwide. Smokers and potential smokers should rely on these messages in making all smoking-related decisions.

http://www.philipmorrisusa.com/DisplayPageWithTopic.asp?ID=60

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Source: https://www.industrydocuments.ucsf.edu/docs/ytlx0001

Purpose

- To compliment the website
- Current view of PM scientists
- Establish reasoning behind PM assessment of causation
- Guidance for future discussions

DOES NOT REVIEW EVIDENCE FOR ANY PARTICULAR DISEASE

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Source: https://www.industrydocuments.ucsf.edu/docs/ytlx0001

Consensus Document Structure:

- Introduction
- Concepts of Causality
- A General Definition of Causation
- Causal Inference in Epidemiology
- The interpretation of evidence on smoking and health
- Areas for future research

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Source: https://www.industrydocuments.ucsf.edu/docs/ytlx0001

Concepts of Causality

- Innate part of human nature
- Seeking to determine consequences of actions
- Desire to change / influence our surroundings
- Level of 'proof' determined by results desired
- Historical debate on causality in health

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Source: https://www.industrydocuments.ucsf.edu/docs/ytlx0001

Definition:

"..an antecedent event, condition, or characteristic that was necessary for the occurrence of the disease at the moment it occurred, given that other conditions are fixed."

Rothman & Greenland, 1997

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Source: https://www.industrydocuments.ucsf.edu/docs/ytlx0001

Implications of this Definition:

- must precede the disease
- absence of a "cause" precludes or postpones the onset of disease
- may not be "sufficient" to produce disease (i.e. only part of a complete causal mechanism)

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CAUSE?

- **A** cause
  - one of a number of components contributing to the effect
- **The** cause
  - the complete combination of component causes inevitably resulting in the effect

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Terminology!

- **Sufficient Cause:**
  - set of minimal conditions & events that inevitably produce disease (each disease may have many…)
- **Component Cause:**
  - one element of a sufficient cause
- **Necessary Cause:**
  - a component cause the absence of which precludes disease development (through all of the sufficient causal mechanisms)

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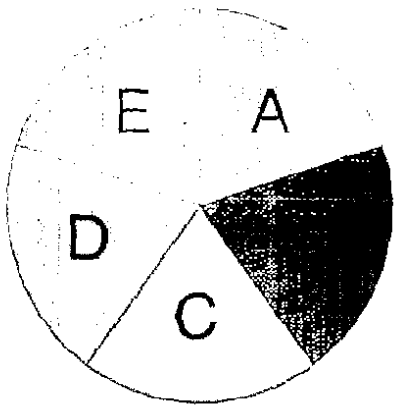
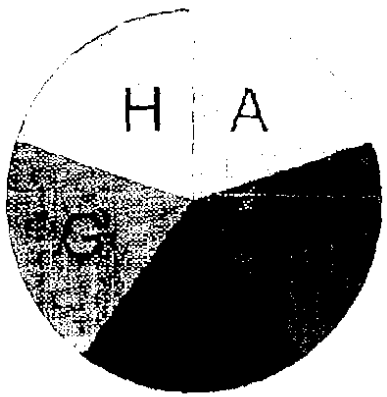
Understanding the Model...

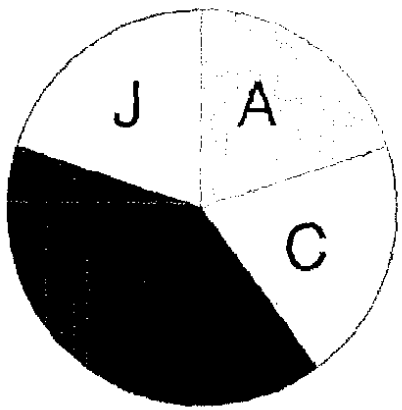
SUFFICIENT CAUSE I



SUFFICIENT CAUSE II



SUFFICIENT CAUSE III



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Understanding the model..

- If sufficient causes I, II & III are the only ones for this hypothetical disease then:
  - 'A' is a "necessary cause"
  - Elimination of any single factor will eliminate the disease associated with the "specific cause(s) in which the factor plays a role.
  - D', 'E', 'G', 'H', 'I' & 'J' only exert an effect in one of the three "sufficient causes"
  - 'B', 'C' & 'F' exert an effect through two of the three "sufficient causes"

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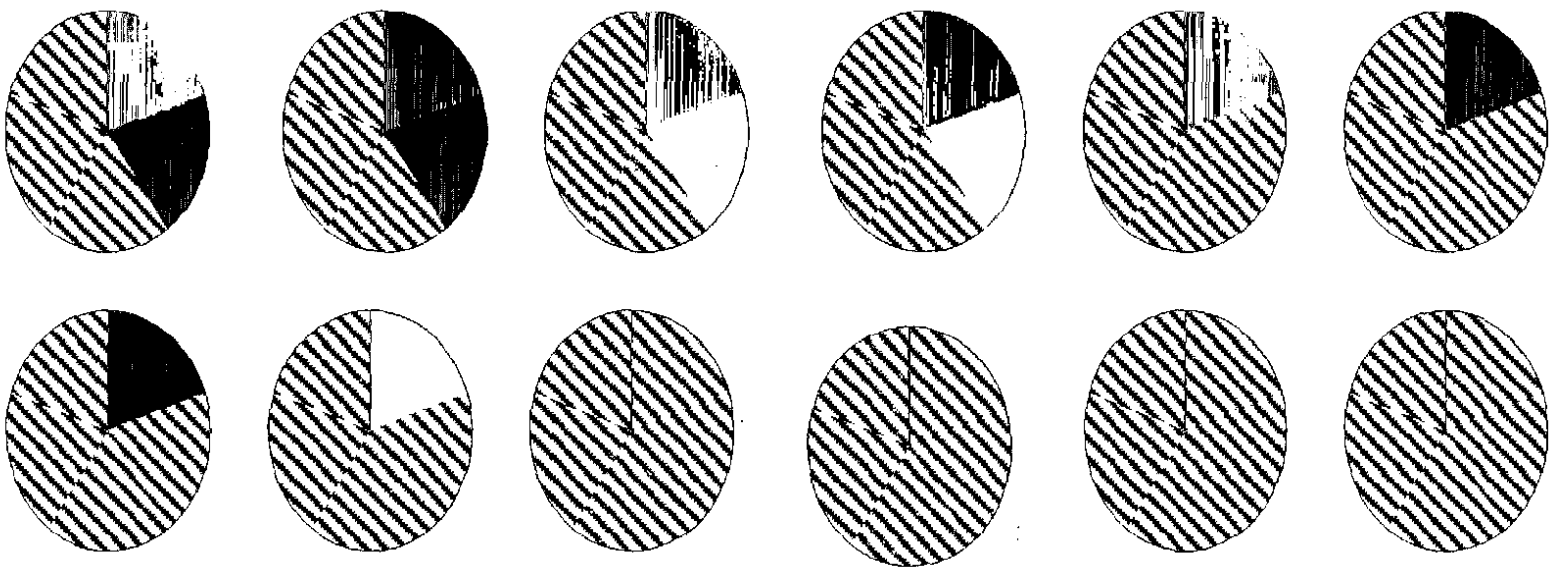
- General model
- details of "component causes" and "sufficient causes" is generally lacking
- applicable to a population
- more likely scenario from current knowledge ....



PMWSA - DRAFT causation presentation - 28 November 2000

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Risk?

- Expresses probability of a given population to succumb to given disease (usually expressed as a rate)
- Individual - actual risk always = 0 or 1
- Population - can be any value between 0 and 1
- In fact we often substitute "population" risks to address "individual" risk for lack of sufficient information to determine individual risk!

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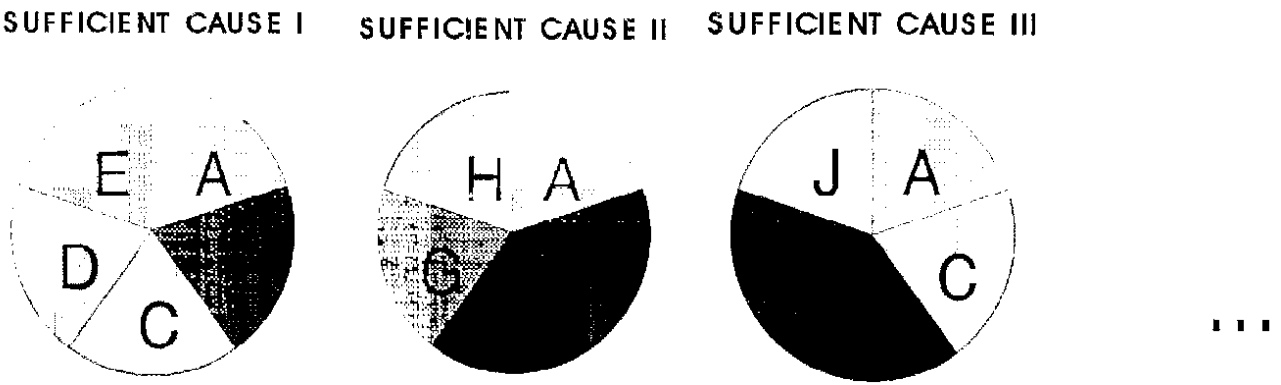
Population:



...

Individual:

Factors present (A) or absent (a)	Probability of disease
A B C D E F G H I J	1
a B C D E F G H I J	0
A B C D E f g h i j	1
A b c d e f g h I j	0
? B ? ? ? ? ? ? ?	P(SCI) + P (SCII)

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Intervention

"In general, it is not necessary to identify all the components of a sufficient cause before effective prevention can take place, since removal of one component may interfere with the action of the others and thus prevent the disease."

Beaglehole et al., "Basic Epidemiology" p71, WHO 1993.

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Causal Inference

- Ultimate proof is elusive
- Process of evaluating the evidence may vary depending on the context
  - "stringency" of proof may be determined by the consequent choice of action
- Therefore requires "Causal Inference"
  - i.e. Application of judgement

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Causal Inference - Tools

Epidemiology

- Extensively used in public health arena
- Interpretation requires the application of judgement
  - Statistical (is the association real?)
  - Causal Inference (is the association causal?)

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Causal Inference - "Aspects"

- After Hill & the US Surgeon General 1964
  - Strength
  - Consistency
  - Specificity
  - Temporality
  - Biological Gradient
  - Plausibility
  - Coherence
  - Experiment
  - Analogy
- Application of such "aspects" can be controversial
- Useful guidance
- **Not** a checklist!

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Source: https://www.industrydocuments.ucsf.edu/docs/ytlx0001

Smoking & Health Contexts:

- Public Health Protection
- Development of Reduced Harm Products

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Public Health:

- Evidence sufficient to support a model in which smoking is a "component cause" for one or more diseases
- Decline in smoking would reasonably be expected to reduce the incidence of such diseases
- Epidemiological evidence largely sufficient to draw such conclusions

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Source: https://www.industrydocuments.ucsf.edu/docs/ytlx0001

Product Development

- Requires understanding of the characteristics of a given product which are linked with the health effect(s)
- Epidemiology identifies the potential health effects
- Understanding of mechanisms necessary to identify potential product modifications
- Requires experimental confirmation of relevant agents and mechanism(s)

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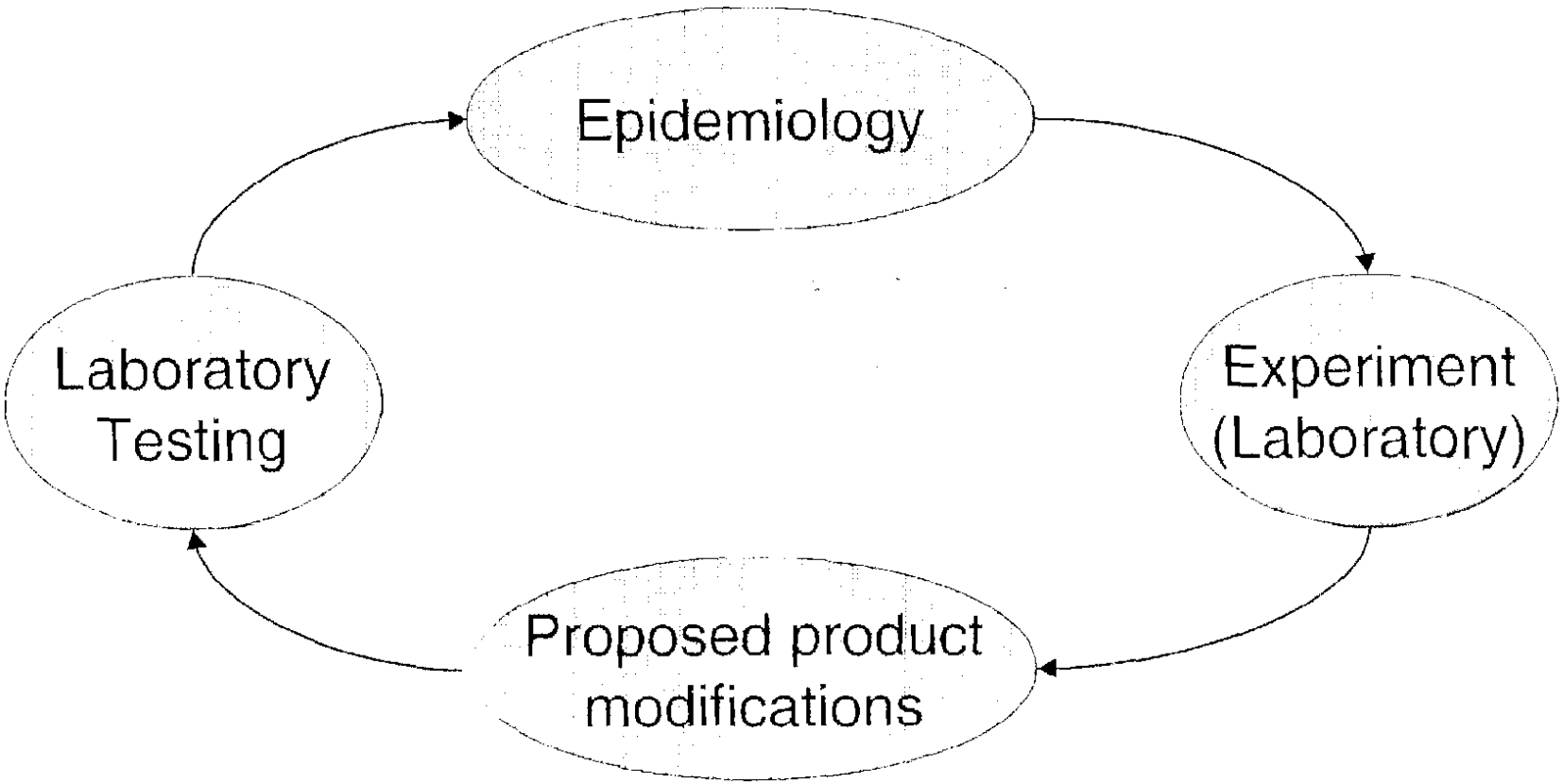
Product Development.



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Areas of future research:

- Susceptible populations
  - identification of some of the unknown causal components
  - provides improvements for testing of future mofications (e.g. population attributes)
  - may help understanding mechanisms
- Direct Mechanisms & Relevant Agents
  - indicate product modifications
- Characterisation of Disease
  - e.g. "Lung Cancer" describes many different diseases
  - specific characterisation of smoking-related diseases may help to clarify specific causal associations.

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Continuation?

- Summary of evidence for individual disease groups?
  - Lung cancer (and subtypes)
  - CVD (and subtypes)
  - COPD (and subtypes)
  - .....others

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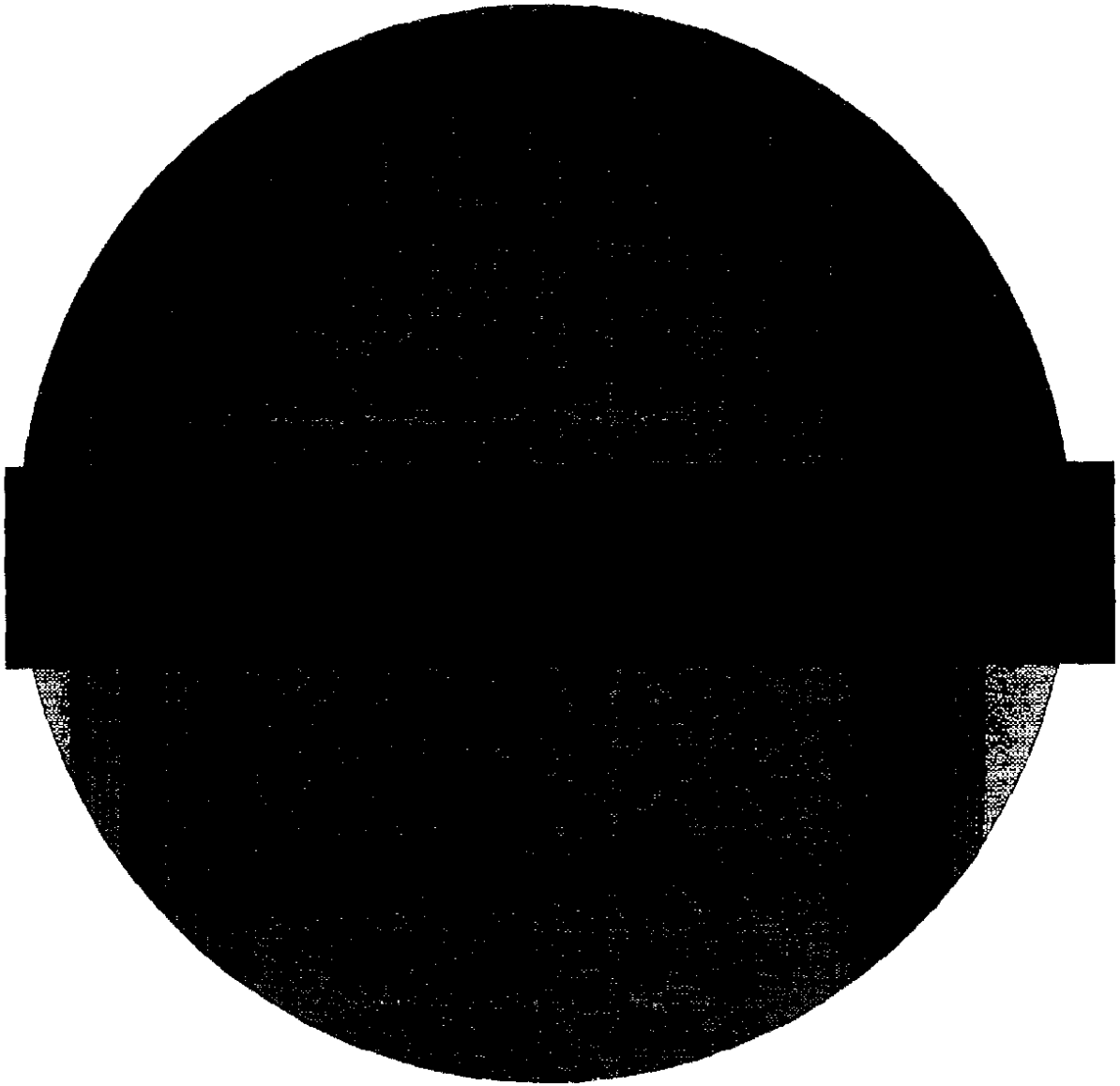

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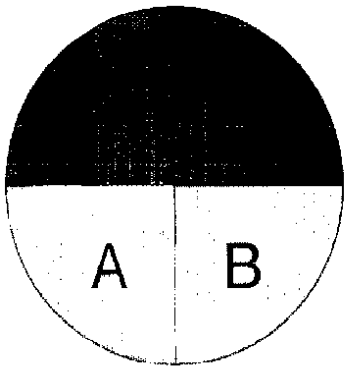
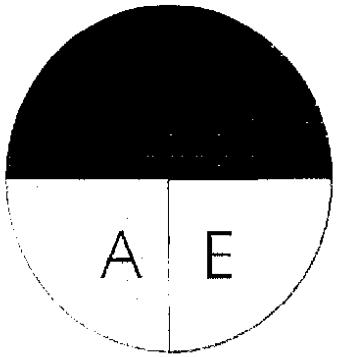
Understanding the Model...

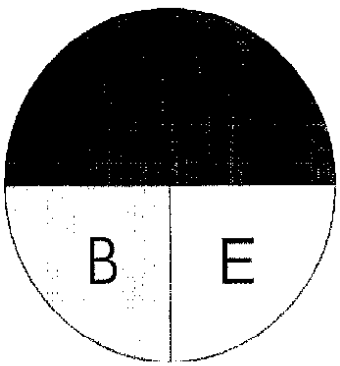
Sufficient Cause I



Sufficient Cause II



Sufficient Cause III



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Strength ...

Exposure frequencies for three component causes in two hypothetical populations according to the possible combinations of the component causes

Exposures:				Response	Frequency of exposure pattern.	
U	A	B	E	(outcome)	Population 1	Population 2
1	1	1	1	1	100	900
1	1	1	0	1	100	900
1	1	0	1	1	900	100
1	1	0	0	0	900	100
1	0	1	1	1	900	100
1	0	1	0	0	900	100
1	0	0	1	0	100	900

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Attributable fraction ...

Pattern of incidence proportions for component causes B & E in hypothetical populations 1 & 2assuming that component cause A is unmeasured.

	B=1, E=1	B=1, E=0	B=0, E=1	B=0, E=0
Population 1:				
Cases	1000	100	900	0
Total	1000	1000	1000	1000
Proportion	1	0.1	0.9	0
Population 2:				
Cases	1000	900	100	0
Total	1000	1000	1000	1000
Proportion	1	0.9	0.1	0

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Attributable fraction:

Population 1:

Of those individuals exposed to B but not E, only 1/10 develop the disease.

Of those individuals exposed to E but not B, 9/10 develop the disease.

Population 2:

Of those individuals exposed to B but not E, 9/10 develop the disease.

Of those individuals exposed to E but not B, only 1/10 develop the diseasse.

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Attributable fraction:

Population 1:

E is a stronger predictor of disease than B.

Population 2:

B is a stronger predictor of disease than E.

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Source: https://www.industrydocuments.ucsf.edu/docs/ytlx0001